

What is Claimed is:

1. An isolated human RNase polypeptide comprising human RNase III.

2. The isolated human RNase polypeptide of claim 1 which comprises an amino acid sequence which is at least 90% homologous to SEQ ID NO: 2.

3. The isolated human RNase polypeptide of claim 1 which comprises the amino acid sequence of SEQ ID NO: 2.

4. A composition which comprises a human RNase III polypeptide and a pharmaceutically acceptable carrier.

5. An isolated polynucleotide which encodes a human RNase III polypeptide.

6. The isolated polynucleotide of claim 5 which comprises a nucleic sequence which is at least 90% homologous to SEQ ID NO: 1.

7. The isolated polynucleotide of claim 5 which comprises the nucleic acid sequence of SEQ ID NO: 1.

8. A vector which comprises a nucleic acid which encodes a human RNase III polypeptide.

9. A host cell which comprises the vector of claim 8.

10. A composition which comprises a vector comprising a nucleic acid encoding a human RNase III polypeptide and a pharmaceutically acceptable carrier.

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11. An antibody targeted to a human RNase III polypeptide.

12. A nucleic acid probe at least 12 nucleobases in length which is capable of hybridizing to a portion
5 of a nucleic acid encoding a human RNase III polypeptide.

13. An antisense compound 8 to 50 nucleobases in length which is targeted to a nucleic acid molecule encoding human RNase III, wherein said antisense
10 compound specifically inhibits the expression of human RNase III.

14. The antisense compound of claim 13 having SEQ ID NO: 8, 9, 10, 11, 12, 13, 14 or 15.

15. A method of inhibiting human RNase III expression or activity in a cell or tissue comprising
15 contacting said cell or tissue with an inhibitor of human RNase III expression or activity.

16. The method of claim 15 wherein the inhibitor of RNase III expression or activity is an antisense
20 compound 8 to 50 nucleobases in length which is targeted to a nucleic acid molecule encoding human RNase III.

17. The method of claim 15 wherein the inhibitor of RNase III expression or activity is an antibody
25 targeted to a human RNase III polypeptide.

18. A method of identifying agents which increase or decrease activity or levels of a human RNase III polypeptide in a host cell comprising:

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(a) contacting a cell expressing a human RNase III polypeptide with an agent suspected of increasing or decreasing activity or levels of the human RNase III polypeptide; and

5 (b) measuring the activity or levels of the human RNase III polypeptide in the presence and absence of the agent so that an increase or decrease in the activity or levels of the human RNase III polypeptide can be determined.

10 19. The composition of claim 4 further comprising an antisense oligonucleotide.

20. A method of promoting inhibition of expression of a selected protein by an antisense oligonucleotide targeted to a target RNA encoding the
15 selected protein comprising:

(a) providing an antisense oligonucleotide targeted to a target RNA encoding a selected protein whose expression is to be inhibited;

(b) allowing said oligonucleotide and said target
20 RNA to hybridize to form an oligonucleotide-target RNA duplex; and

(c) contacting said oligonucleotide-target RNA duplex with an RNase III polypeptide, under conditions in which cleavage of the target RNA strand of the
25 oligonucleotide-target RNA duplex by the RNase III polypeptide occurs,

whereby inhibition of expression of the selected protein is promoted.

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21. The method of claim 20 wherein the RNase III polypeptide is a human RNase III polypeptide.

22. The method of claim 21 wherein the human RNase III polypeptide comprises an amino acid sequence which
5 is at least 90% homologous to SEQ ID NO: 2.

23. The method of claim 21 wherein the human RNase III polypeptide comprises the amino acid sequence of SEQ ID NO: 2.

24. The method of claim 20 wherein the antisense
10 oligonucleotide is an RNA-like oligonucleotide.

25. The method of claim 24 wherein the RNA-like oligonucleotide has a modification at the 2' position of at least one sugar.

26. The method of claim 20 wherein the RNase III
15 polypeptide is present in enriched amounts.

27. The method of claim 26 wherein the RNase III polypeptide present in enriched amounts is overexpressed or exogenously added.

28. The method of claim 27 wherein the RNase III
20 polypeptide is an isolated, purified RNase III polypeptide.

29. A method of screening oligonucleotides to identify effective antisense oligonucleotides for inhibition of expression of a selected target protein
25 comprising:

(a) contacting a human RNase III polypeptide with a target RNA encoding the selected target protein and an oligonucleotide complementary to at least a portion

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of the target RNA under conditions in which an oligonucleotide-target RNA duplex is formed;

(b) detecting cleavage of the target RNA of the oligonucleotide-target RNA duplex wherein cleavage is
5 indicative of antisense efficacy.

30. The method of claim 29 further comprising determining the site on the target RNA at which cleavage occurs, whereby said site is identified as an RNase III-sensitive site.

10 31. The method of claim 29 further comprising identifying an effective antisense oligonucleotide which hybridizes to said RNase III-sensitive site.

32. The method of claim 29 wherein the oligonucleotide is one of a mixture or library of
15 oligonucleotides.

33. The method of claim 29 wherein the oligonucleotide is an RNA-like oligonucleotide.

34. The method of claim 33 wherein the RNA-like oligonucleotide has a modification at the 2' position
20 of at least one sugar.

35. A method of prognosticating efficacy of antisense therapy of a selected disease comprising measuring the level or activity of a human RNase III in a target cell of the antisense therapy.

25 36. A method of identifying agents which increase or decrease activity or levels of a human RNase III polypeptide in a host cell comprising:

(a) contacting a cell expressing a human RNase III polypeptide with an agent suspected of increasing or

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decreasing activity or levels of the human RNase III polypeptide; and

(b) measuring the activity or levels of the human RNase III polypeptide in the presence and absence of the agent so that an increase or decrease in the activity or levels of the human RNase III polypeptide can be determined.

37. A method of eliciting cleavage of a selected cellular RNA target comprising:

(a) providing an antisense oligonucleotide targeted to a selected cellular RNA target to be cleaved, wherein said oligonucleotide is an RNA-like oligonucleotide;

(b) allowing said oligonucleotide and said RNA to hybridize to form an oligonucleotide-RNA duplex; and

(c) contacting said oligonucleotide-RNA duplex with an RNase III polypeptide, under conditions in which cleavage of the oligonucleotide-RNA duplex by the RNase III polypeptide occurs,

whereby cleavage of the cellular RNA target is elicited.

38. The method of claim 37 wherein the RNase III polypeptide is a human RNase III polypeptide.

39. The method of claim 37 wherein the RNase III polypeptide is present in enriched amounts.

40. The method of claim 39 wherein the RNase III polypeptide present in enriched amounts is overexpressed or exogenously added.

41. The method of claim 37 wherein the RNase III polypeptide is an isolated, purified RNase III polypeptide.

42. The method of claim 37 wherein the RNA-like
5 oligonucleotide has a modification at the 2' position of at least one sugar.

43. A method of promoting RNA interference in a cell comprising providing to said cell an RNase III polypeptide in amounts sufficient to promote RNA
10 interference.

44. The method of claim 43 wherein said RNase III polypeptide is exogenously added.

45. The method of claim 43 wherein said RNase III polypeptide is an isolated, purified RNase III
15 polypeptide.

46. The method of claim 43 wherein said RNase III polypeptide is expressed by an exogenously added vector encoding said RNase III polypeptide.

47. The method of claim 43 wherein said cell or
20 animal is a human cell.

48. A method of promoting RNA interference in a cell comprising enriching the amount or activity of RNase III polypeptide in said cell to a level sufficient to promote RNA interference.

49. The method of claim 48 wherein said enriching
25 is by exogenous addition of RNase III polypeptide.

50. The method of claim 49 wherein said exogenously added RNase III polypeptide is an isolated, purified RNase III polypeptide.

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51. The method of claim 48 wherein said enriching is by an exogenous addition of a vector encoding said RNase III polypeptide.

52. The method of claim 48 wherein said cell or
5 animal is a human cell.

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